



REL Appalachia Ask A REL Response

Behavior and Mental Health

December 2019

Question:

How does K–12 students' proper use of prescribed medications relate to later substance abuse and misuse?

Response:

Thank you for your request to our REL Reference Desk regarding evidence-based information about how students' proper use of prescription medication may impact later substance abuse and misuse. Ask A REL is a collaborative reference desk service provided by the 10 Regional Educational Laboratories (RELs) that, by design, functions much in the same way as a technical reference library. Ask A REL provides references, referrals, and brief responses in the form of citations in response to questions about available education research.

Following an established REL Appalachia research protocol, we searched for peer-reviewed articles and other research reports on prescription medication and later substance abuse and misuse. We focused on identifying resources that specifically addressed how students' proper use of prescription medication relates to later substance abuse and misuse. The sources included ERIC and other federally funded databases and organizations, research institutions, academic research databases, and general Internet search engines. For more details, please see the methods section at the end of this document.

The research team did not evaluate the quality of the resources provided in this response; we offer them only for your reference. Also, the search included the most commonly used research databases and search engines to produce the references presented here, but the references are not necessarily comprehensive, and other relevant references and resources may exist. References are listed in alphabetical order, not necessarily in order of relevance.

References

Boyd, C. J., Meier, E. A., Epstein-Ngo, Q., Veliz, P. T., & McCabe, S. E. (2015). A prospective study of adolescents' nonmedical use of anxiolytic and sleep medication. *Psychology of Addictive Behaviors, 29*(1), 184–191. Retrieved from

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4388758/pdf/nihms639187.pdf>

From the abstract: “The purpose of this longitudinal study ($N = 2,745$) was to determine whether adolescents’ recent medical use of anxiolytic or sleep medication was associated with increased incidence of using someone else’s prescription for these classes of medication (nonmedical use). Data were collected from adolescents attending five Detroit area secondary schools between December and April in three consecutive academic years between 2009 and 2012. Respondents were assigned to the following three mutually exclusive groups for the analyses: 1) never prescribed anxiolytic or sleep medication (in their lifetime); 2) prescribed anxiolytic or sleep medication in their lifetime, but not during the study period; or 3) prescribed anxiolytic or sleep medication during the study period. Almost 9% of the sample had received a prescription for anxiolytic or sleep medication during their lifetime and 3.4% had received at least one prescription during the three-year study period. Compared with adolescents never prescribed anxiolytic or sleep medication, adolescents prescribed these medicines during the study period were 10 times more likely to engage in nonmedical use for reasons such as ‘to get high’ or to experiment (Adjusted Odds Ratio [AOR], 10.15 [95% CI, 3.97–25.91]), and 3 times more likely to engage in nonmedical use to self-treat anxiety or to sleep (AOR, 3.24 [95% CI, 1.67–6.29]). Adolescents prescribed anxiolytics during their lifetime, but not during the three-year study, were 12 times more likely to use another’s anxiolytic medication, compared to adolescents never prescribed anxiolytics (AOR, 12.17 [95% CI, 3.98–37.18]). These risk factors have significant implications for later substance use problems.”

Harstad, E., Levy, S., & Committee on Substance Abuse (2014). Attention-deficit/hyperactivity disorder and substance abuse. *Pediatrics*, *134*(1), 293–301. Retrieved from <https://themaribelgonzalez.com/wp-content/uploads/2018/02/ADHD-and-Substance-Use-Disorder AAP 2014-1.pdf>

From the abstract: “Attention-deficit/hyperactivity disorder (ADHD) and substance use disorders are inextricably intertwined. Children with ADHD are more likely than peers to develop substance use disorders. Treatment with stimulants may reduce the risk of substance use disorders, but stimulants are a class of medication with significant abuse and diversion potential. The objectives of this clinical report were to present practical strategies for reducing the risk of substance use disorders in patients with ADHD and suggestions for safe stimulant prescribing.”

Humphreys, K. L., Eng, T., & Lee, S. S. (2013). Stimulant medication and substance use outcomes: A meta-analysis. *JAMA Psychiatry*, 1–9. Retrieved from https://leelab.psych.ucla.edu/wp-content/uploads/sites/44/2015/10/Humphreys_2013_Stimulant.pdf

From the abstract: “Importance: Psychostimulant medication is an efficacious treatment for childhood attention-deficit/hyperactivity disorder, yet controversy remains regarding potential iatrogenic effects of stimulant medication, particularly with respect to increasing susceptibility to later substance use disorders. However, stimulant treatment was previously reported to reduce the risk of substance problems. Objective: To meta-analyze the longitudinal association between treatment with stimulant medication during childhood

and later substance outcomes (i.e., lifetime substance use and substance abuse or dependence). Data Sources: Studies published between January 1980 and February 2012 were identified using review articles, PubMed, and pertinent listservs. Study Selection: Studies with longitudinal designs in which medication treatment preceded the measurement of substance outcomes. Data Extraction and Synthesis: Odds ratios were extracted or provided by the study authors. Odds ratios were obtained for lifetime use (ever used) and abuse or dependence status for alcohol, cocaine, marijuana, nicotine, and nonspecific drugs for 2565 participants from 15 different studies. Main Outcomes and Measures: Random-effects models estimated the overall association, and potential study moderators were examined. Results: Separate random-effects analyses were conducted for each substance outcome, with the number of studies ranging from 3 to 11 for each outcome. Results suggested comparable outcomes between children with and without medication treatment history for any substance use and abuse or dependence outcome across all substance types. Conclusions: These results provide an important update and suggest that treatment of attention-deficit/hyperactivity disorder with stimulant medication neither protects nor increases the risk of later substance use disorders.”

Lee, S. S., Humphreys, K. L., Flory, K., Liu, R., & Glass, K. (2011). Prospective association of childhood attention-deficit/hyperactivity disorder (ADHD) and substance use and abuse/dependence: A meta-analytic review. *Clinical Psychology Review, 31*(3), 328–341. Retrieved from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3180912/pdf/nihms314363.pdf>

From the abstract: “Given the clinical and public health significance of substance disorders and the need to identify their early risk factors, we examined the association of childhood attention-deficit/hyperactivity disorder (ADHD) with substance use (nicotine, alcohol, marijuana) and abuse/dependence outcomes (nicotine, alcohol, marijuana, cocaine, other). To strengthen a potential causal inference, we meta-analyzed longitudinal studies that prospectively followed children with and without ADHD into adolescence or adulthood. Children with ADHD were significantly more likely to have ever used nicotine and other substances, but not alcohol. Children with ADHD were also more likely to develop disorders of abuse/dependence for nicotine, alcohol, marijuana, cocaine, and other substances (i.e., unspecified). Sex, age, race, publication year, sample source, and version of the Diagnostic and Statistical Manual of Mental Disorders (DSM) used to diagnose ADHD did not significantly moderate the associations with substance outcomes that yielded heterogeneous effect sizes. These findings suggest that children with ADHD are significantly more likely to develop substance use disorders than children without ADHD and that this increased risk is robust to demographic and methodological differences that varied across the studies. Finally, few studies addressed ADHD and comorbid disruptive behavior disorders (DBD), thus preventing a formal meta-analytic review. However, we qualitatively summarize the results of these studies and conclude that comorbid DBD complicates inferences about the specificity of ADHD effects on substance use outcomes.”

McCabe, S. E., Veliz, P., & Boyd, C. J. (2016). Early exposure to stimulant medications and substance-related problems: The role of medical and nonmedical contexts. *Drug and*

Alcohol Dependence, 163, 55–63. Retrieved from

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4921894/pdf/nihms776584.pdf>

From the abstract: “Background: The age of onset (early vs. late) and context (medical vs. nonmedical) of exposure to stimulant medications for attention-deficit/hyperactivity disorder (ADHD) have been identified as important factors in the addictive potential of these controlled medications. This study examines the role of medical and nonmedical contexts in the association between early exposure to stimulant medications and substance use and substance-related problems among adolescents. Methods: A Web-based survey was self-administered by Detroit-area secondary school students ($N = 4,755$) between the 2009–10 and 2012–13 school years. The sample consisted of 51% females, 62% Whites, 32% African-Americans, and 6% from other racial categories. Results: During the study period, an estimated 11.7% of respondents were ever diagnosed with ADHD. Approximately 6.7% ($n = 322$) of respondents indicated lifetime medical use of prescription stimulants while 2.6% ($n = 124$) indicated lifetime nonmedical use. The odds of substance use and substance-related problems were significantly lower among those who initiated earlier medical use of stimulant medications relative to later medical initiation. In contrast, the odds of substance use and substance-related problems were significantly greater among those who initiated earlier nonmedical use of stimulant medications relative to later nonmedical initiation. Conclusions: More than one in every ten adolescents in this epidemiologically-derived community-based sample was diagnosed with ADHD. This is the first investigation to demonstrate that context (medical vs. nonmedical) plays a critical role in the relationship between early exposure to stimulant medications and the subsequent risk of substance-related problems during adolescence within the same diverse youth sample.”

McCabe, S. E., Veliz, P., Boyd, C. J., & Schulenberg, J. E. (2016). Medical and nonmedical use of prescription sedatives and anxiolytics: Adolescents’ use and substance use disorder symptoms in adulthood. *Addictive Behaviors*, 65, 296–301. Retrieved from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5462596/>

From the abstract: “Objectives: This study assessed the longitudinal associations between medical and nonmedical use of prescription sedatives/anxiolytics (NMPSA) during adolescence (age 18) and substance use disorder (SUD) symptoms during adulthood (age 35). Methods: Multiple cohorts of nationally representative samples of U.S. high school seniors ($n = 8,373$) were surveyed via self-administered questionnaires and followed longitudinally from adolescence (age 18, 1976–1996) to adulthood (age 35, 1993–2013). Results: An estimated 20.1% of adolescents reported lifetime medical or nonmedical use of prescription sedatives/anxiolytics. Among adolescents who reported medical use of prescription sedatives/anxiolytics, 44.9% also reported NMPSA by age 18. Based on multivariate analyses that included age 18 sociodemographic and other substance use controls, medical use of prescription sedatives/anxiolytics without any history of NMPSA during adolescence was not associated with SUD symptoms in adulthood relative to adolescents with no prescription sedative/anxiolytic use. In contrast, adolescents with a history of both medical and nonmedical use of prescription sedatives/anxiolytics and adolescents who reported only NMPSA had between two to three times greater odds of

SUD symptoms in adulthood relative to adolescents with no prescription sedative/anxiolytic use and those who reported only medical use of prescription sedatives/anxiolytics.

Conclusions: One in every five U.S. high school seniors report ever using prescription sedatives/anxiolytics either medically or nonmedically. This study provides compelling evidence that the medical use of prescription sedatives/anxiolytics (without any NMPSA) during adolescence is not associated with increased risk of SUD symptoms in adulthood while any NMPSA during adolescence serves as a signal for SUDs in adulthood.”

McCabe, S. E., & West, B. T. (2014). Medical and nonmedical use of prescription benzodiazepine anxiolytics among U.S. high school seniors. *Addictive Behaviors, 39*(5), 959–964. Retrieved from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4312492/pdf/nihms-568276.pdf>

From the abstract: “Objectives: To examine the lifetime prevalence of medical and nonmedical use of prescription benzodiazepine anxiolytics among U.S. high school seniors and to assess substance use behaviors based on lifetime histories of medical and nonmedical use of prescription benzodiazepine anxiolytics. Methods: Nationally representative samples of high school seniors were surveyed during their senior year via self-administered questionnaires. The sample consisted of 11,248 high school seniors (modal age 18 years) from five independent cohorts (2007–2011). The sample was 52% female, 65% White, 12% African-American, 15% Hispanic, and 7% other. Results: The lifetime prevalence of medical use of prescription benzodiazepine anxiolytics was 4.9%, while the lifetime prevalence of nonmedical use was 7.5%. Although lifetime prevalence rates were relatively stable over time, there were notable sex and racial/ethnic differences in medical and nonmedical use behaviors. Among those who were ever prescribed benzodiazepine anxiolytics ($n = 530$), approximately 40.6% reported medical use only, 27.4% reported medical use prior to nonmedical use, and 32.0% reported nonmedical use prior to medical use. The odds of substance use behaviors were greater among those who reported any history of nonmedical use relative to non-users while the odds of substance use behaviors did not differ between medical users only and non-users. Conclusions: One in every ten U.S. high school seniors has ever had some exposure to prescription benzodiazepine anxiolytics either medically or nonmedically. Benzodiazepine anxiolytics prescribed to adolescents should be closely monitored, safely stored, and properly disposed to reduce nonmedical use due to leftover medication and peer diversion.”

McCabe, S. E., West, B. T., & Boyd, C. J. (2013). Motives for medical misuse of prescription opioids among adolescents. *Journal of Pain, 14*(10), 1208–1216. Retrieved from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3792708/pdf/nihms483662.pdf>

From the abstract: “This study examined the motives for medical misuse of prescription opioids among adolescents, and assessed differences in motives by demographic characteristics, substance abuse, and diversion behaviors. A survey was conducted in 2011–2012 and the sample consisted of 2,964 adolescents (51% female). Thirteen percent reported past-year medical use of prescription opioids. Among those prescribed opioids in the past-year ($n = 393$), 17.9% reported medical misuse (e.g., using too much, to get high, or to increase alcohol or other drug effects). The most prevalent motives for medical misuse

were 'to relieve pain' (84.2%) and 'to get high' (35.1%). Multivariate analyses indicated that the motives differed by race, and that different motives were associated with different substance abuse and diversion behaviors. The odds of past-year substance abuse among medical misusers motivated by non-pain relief were over *fifteen* times greater than for nonusers (AOR = 15.2, 95% CI = 6.4 – 36.2, $p < .001$). No such differences existed between nonusers and appropriate medical users, or between nonusers and medical misusers motivated by pain relief only. These findings improve our understanding of opioid medication misuse among adolescents and indicate the need for enhanced education about appropriate medical use, pain management, and patient communication with prescribers.”

Miech, R., Johnston, L., O'Malley, P. M., Keyes, K. M., & Heard, K. (2015). Prescription opioids in adolescence and future opioid misuse. *Pediatrics*, *136*(5), 1169–1177. Retrieved from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4834210/pdf/peds.2015-1364.pdf>

From the abstract: “Background and objective: Legitimate opioid use is associated with an increased risk of long-term opioid use and possibly misuse in adults. The objective of this study was to estimate the risk of future opioid misuse among adolescents who have not yet graduated from high school. Methods: Prospective, panel data come from the Monitoring the Future study. The analysis uses a nationally representative sample of 6220 individuals surveyed in school in 12th grade and then followed up through age 23. Analyses are stratified by predicted future opioid misuse as measured in 12th grade on the basis of known risk factors. The main outcome is nonmedical use of a prescription opioid at ages 19 to 23. Predictors include use of a legitimate prescription by 12th grade, as well as baseline history of drug use and baseline attitudes toward illegal drug use. Results: Legitimate opioid use before high school graduation is independently associated with a 33% increase in the risk of future opioid misuse after high school. This association is concentrated among individuals who have little to no history of drug use and, as well, strong disapproval of illegal drug use at baseline. Conclusions: Use of prescribed opioids before the 12th grade is independently associated with future opioid misuse among patients with little drug experience and who disapprove of illegal drug use. Clinic-based education and prevention efforts have substantial potential to reduce future opioid misuse among these individuals, who begin opioid use with strong attitudes against illegal drug use.”

Molina, B. S. G., Hinshaw, S. P., Eugene Arnold, L., Swanson, J. M., Pelham, W. E., Hechtman, L., ... MTA Cooperative Group. (2013). Adolescent substance use in the multimodal treatment study of attention-deficit/hyperactivity disorder (ADHD) (MTA) as a function of childhood ADHD, random assignment to childhood treatments, and subsequent medication. *Journal of the American Academy of Child and Adolescent Psychiatry*, *52*(3), 250–263. Retrieved from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3589108/pdf/nihms431581.pdf>

From the abstract: “Objective: To determine long-term effects on substance use and substance use disorder (SUD), up to 8 years after childhood enrollment, of the randomly assigned 14-month treatments in the multisite Multimodal Treatment Study of Children with Attention-Deficit/Hyperactivity Disorder (MTA; $n = 436$); to test whether medication at follow-up, cumulative psychostimulant treatment over time, or both relate to substance

use/SUD; and to compare substance use/SUD in the ADHD sample to the non-ADHD childhood classmate comparison group ($n = 261$). Method: Mixed-effects regression models with planned contrasts were used for all tests except the important cumulative stimulant treatment question, for which propensity score matching analysis was used. Results: The originally randomized treatment groups did not differ significantly on substance use/SUD by the 8-year follow-up or earlier (mean age = 17 years). Neither medication at follow-up (mostly stimulants) nor cumulative stimulant treatment was associated with adolescent substance use/SUD. Substance use at all time points, including use of two or more substances and SUD, were each greater in the ADHD than in the non-ADHD samples, regardless of sex. Conclusions: Medication for ADHD did not protect from, or contribute to, visible risk of substance use or SUD by adolescence, whether analyzed as randomized treatment assignment in childhood, as medication at follow-up, or as cumulative stimulant treatment over an 8-year follow-up from childhood. These results suggest the need to identify alternative or adjunctive adolescent-focused approaches to substance abuse prevention and treatment for boys and girls with ADHD, especially given their increased risk for use and abuse of multiple substances that is not improved with stimulant medication.”

Winters, K. C., Lee, S., Botzet, A., Fahnhorst, T., Realmuto, G. M., & August, G. J. (2011). A prospective examination of the association of stimulant medication history and drug use outcomes among community samples of ADHD youths. *Journal of Child & Adolescent Substance Abuse*, 20(4), 314–329. Retrieved from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3348651/pdf/nihms371830.pdf>

From the abstract: “A continuing debate in the child psychopathology literature is the extent to which pharmacotherapy for children with attention-deficit/hyperactivity disorder (ADHD), in particular stimulant treatment, confers a risk of subsequent drug abuse. If stimulant treatment for ADHD contributes to drug abuse, then the risk versus therapeutic benefits of such treatment is greatly affected. We have prospectively followed an ADHD sample ($N = 149$; 81% males) for approximately 15 years, beginning at childhood (ages 8 to 10 years) and continuing until the sample has reached young adulthood (ages 22 to 24 years). The sample was originally recruited via an epidemiologically derived community procedure, and all youths were diagnosed with ADHD during childhood. We report on the association of childhood psychostimulant medication and subsequent substance use disorders and tobacco use. The substance use outcomes were based on data collected at three time points when the sample was in late adolescence and young adulthood (age range approximately 18 to 22 years old). We did not find evidence to support that childhood treatment with stimulant medication, including the course of stimulant medication, was associated with any change in risk for adolescent or young adulthood substance use disorders and tobacco use. These results from a community-based sample extend the growing body of literature based on clinically derived samples indicating that stimulant treatment does not create a significant risk for subsequent substance use disorders.”

Additional Organizations to Consult

National Institute on Drug Abuse: <https://www.drugabuse.gov/>

From the website: “Our mission is to advance science on the causes and consequences of drug use and addiction and to apply that knowledge to improve individual and public health. This involves:

- Strategically supporting and conducting basic and clinical research on drug use (including nicotine), its consequences, and the underlying neurobiological, behavioral, and social mechanisms involved.
- Ensuring the effective translation, implementation, and dissemination of scientific research findings to improve the prevention and treatment of substance use disorders and enhance public awareness of addiction as a brain disorder.”

Partnership for Drug-Free Kids: <https://drugfree.org/>

From the website: “We are the go-to organization for families addressing every aspect of substance use and addiction, from prevention to recovery. We empower parents and caregivers with support and guidance using the latest science-based information. We research and advance effective prevention and treatment strategies. We advocate for lifesaving policy changes. Finally, we aspire to change the national conversation around addiction so that no one will feel alone or ashamed to seek help, and everyone has access to the care they need and deserve... In 2019, we merged with Center on Addiction, and together, our mission is to transform how the nation addresses addiction.”

Substance Abuse and Mental Health Services Administration (SAMHSA):

<https://www.samhsa.gov/>

From the website: “The Substance Abuse and Mental Health Services Administration (SAMHSA) is the agency within the U.S. Department of Health and Human Services that leads public health efforts to advance the behavioral health of the nation. SAMHSA’s mission is to reduce the impact of substance abuse and mental illness on America’s communities.”

Methods

Keywords and Search Strings

The following keywords and search strings were used to search the reference databases and other sources:

- (child* OR youth OR adolescen*) AND (“prescription drug” OR “prescription medication”) AND (“substance abuse” OR “later substance abuse” OR “substance misuse”)

- (child* OR youth OR adolescen*) AND (“prescribed opioid” OR “prescribed sedative” OR “prescribed anxiolytic” OR “prescribed benzodiazepine”) AND (“substance misuse” OR “substance abuse” OR “nonmedical use”)

Databases and Resources

We searched ERIC, a free online library of more than 1.6 million citations of education research sponsored by the Institute of Education Sciences (IES), for relevant resources. Additionally, we searched the academic database ProQuest, Google Scholar, and the commercial search engine Google.

Reference Search and Selection Criteria

In reviewing resources, Reference Desk researchers consider—among other things—these four factors:

- Date of the publication: Searches cover information available within the last ten years, except in the case of nationally known seminal resources.
- Reference sources: IES, nationally funded, and certain other vetted sources known for strict attention to research protocols receive highest priority. Applicable resources must be publicly available online and in English.
- Methodology: The following methodological priorities/considerations guide the review and selection of the references: (a) study types—randomized controlled trials, quasi experiments, surveys, descriptive data analyses, literature reviews, policy briefs, etc., generally in this order; (b) target population, samples (representativeness of the target population, sample size, volunteered or randomly selected), study duration, etc.; (c) limitations, generalizability of the findings and conclusions, etc.
- Existing knowledge base: Vetted resources (e.g., peer-reviewed research journals) are the primary focus, but the research base is occasionally slim or nonexistent. In those cases, the best resources available may include, for example, reports, white papers, guides, reviews in non-peer-reviewed journals, newspaper articles, interviews with content specialists, and organization websites.

Resources included in this document were last accessed on November 15, 2019. URLs, descriptions, and content included here were current at that time.

This memorandum is one in a series of quick-turnaround responses to specific questions posed by education stakeholders in the Appalachia region (Kentucky, Tennessee, Virginia, and West Virginia), which is served by the Regional Educational Laboratory Appalachia (REL AP) at SRI International. This Ask A REL response was developed by REL AP under Contract ED-IES-17-C-0004 from the U.S. Department of Education, Institute of Education Sciences, administered by SRI International. The content does not necessarily reflect the views or policies of IES or the U.S. Department of Education, nor does mention of trade names, commercial products, or organizations imply endorsement by the U.S. government.